DOI Number: 10.37506/v11/i1/2020/ijphrd/194064

The Effect of Olanzapine on the Improvement of the Clinical Symptom of Schizophrenia

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Abstract

Administration of atypicalantipsychotics (risperidone, olanzapine and clozapine) can improve cognitive dysfunction which occurs in schizophrenia patients. This study was aimed at analyzing the effect of olanzapine on the improvement of clinical symptom (the positive and negative symptoms) in schizophrenia patients. The study was observational with analytic approach on inpatient and outpatient schizophrenia patients in Wahidin Sudirohusodo Hospital and its networking. Subjects comprised of 30 samples who were divided into two groups: the risperidone group which consisted of 15 subjects and the olanzapine group which consisted of 15 subjects. The positive and the negative Symptom Scale (PANSS) wasused to evaluate the psychopathological symptoms. The results showed that improvement of clinical symptom based on the decrease of the positive symptom of thePANSS was significant ($p<0.05$) since the 2nd week in both groups. However, comparison of the changes of the positive symptom of the PANSS after medical treatment showed that the decrease of the positive symptom of the PANSS was greater in the risperidone group compared to the olanzapine group ($p<0,05$). As for negative symptom of the PANSS between the two treatment groups showed that the decrease of negative symptom of the PANSS was significant ($p<0.05$) since the 2nd week.

Keywords: *Risperidone, olanzapine, clozapine, positive and negative symptoms, Schizophrenia.*

Background

The course of schizophrenia consists of three phases. The first phase is the acute phase, characterized by the emergence of positive and negative symptoms, then followed by a stabilization phase, characterized by the relief of a symptom, and then a stable phase, characterized by reduced symptom severity.[1] Schizophrenia is a chronic, severe, pervasive mental disorder, which is characterized by hallucinations, delusions, and impairments in reality assessment. This disorder has a profound and influential impact on many lives and ultimately affects the quality of life of patients.[5,2] Several studies have been conducted to compare the advantages of atypical antipsychotics, since atypical antipsychotics have a brood effect in reducing psychotic symptoms with lower extra pyramidal side effects, leading to a better quality of life than typical antipsychotics.[3] Until now, schizophrenia was known as chronic disease. At the beginning, the goal of therapy is to control positive and negative symptoms in schizophrenia. A data published in 2013 showed that the prevalence of severe mental disorders in Indonesia such as schizophrenia reached around 400,000 people or 1.7 per 1,000 population, overall there was 1% of the population in the world who suffered from schizophrenia.[7]

Oral atypical antipsychotics are considered as the first line treatment, especially for people with newly diagnosed schizophrenia.[9] Atypical antipsychotics are also referred to as second generation antipsychotic (SGA). Included in this class of drugs are risperidone, olanzapine, quetiapine, clozapine and ziprasidone. SGA can suppress positive symptoms, improve cognitive dysfunction, improvesymptom which are refractory to

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typical antipsychotic treatment by blocking more 5HT2A receptor than dopamine inmesocortical pathway. SGA also blocks D2 receptors, resulting in more dopamine being released in the mesocortical pathway and causing an improvement in negative symptoms of schizophrenia. However, the affinity of each drug varies with various types of neurotransmitter receptors which in turn give different therapeutic profiles.[10,11,12]

Risperidone can improve schizophrenia, improve mood in schizophrenia and bipolar disorder. Serotonin has an important role in influencing dopamine but has different effects on each dopamine pathway. Serotonin inhibition occurs in the mesocortex pathway resulting in the release of dopamine in the body cells and axon terminal at post-synapse. This is why risperidone could improve negative symptom.[10]Lately, the use of atypical antipsychotic drugs was more often, with minimal side effect and could improve the positive and negative symptoms of schizophrenia patients.

Previous research[6,8]compared the administration of risperidoneand olanzapine therapy in schizophrenic patients. The results showed improvement for clinical symptoms of schizophrenia patients, especially the negative symptoms of patients who received olanzapine therapy compared to those who received risperidone therapy, meanwhile the administration of risperidone showed improvement in positive symptoms of schizophrenia compare to those who received olanzapine therapy. Since it is importance to determine the right antipsychotic from the beginning of therapy to ensure a good response for the improvement of symptoms of schizophrenic patients, researchers were interested in comparing the effectiveness of the two types of atypical antipsychotics most commonly used in Makassar, which arerisperidone and olanzapine. So far, there had never been any research on the comparison of these two types of drugs based on the positive and negative symptoms of general psychopathology of schizophrenia.

Materials and Method

Location and Time of Research: The study was conducted at Wahidin Sudirohusodo Hospital and its network and from June to August 2018. This study was an analytic observational study. Subjects of the study were schizophrenia patients who were inpatient and outpatient who met the inclusion and exclusion criterias.

Method of data collection: Every schizophrenia patients who met the inclusion criteria was included in the study and data was taken including name, gender, age, last education, occupation,history of the objects previous diseases. The subjects were divided into two groups, risperidone group treatment (group A), and olanzapine group (treatment group B).Each objects from both groups were assessed for PANSS scores before being given therapy with olanzapine or risperidone. The positive symptom of the PANSS and the negative symptom of the PANSS scores were assessed for both groups in the 4th and 8th week.

*All data wa*s processed and analyzed by statistic program.

Results

Thirty subjects joined the study, consist of fifteen subjects who were given risperidone and fifteen subjects who were given olanzapine. The risperidone group was given 2 mg each 12 hours orally and the olanzapine was given10 mg each 24 hours orally. Measurement of PANSS scores for each subject was carried out at baseline, on the 2nd week,on the 4th week and on the 8th week of therapy.

The change of the positive symptom of the PANSS score inrisperi done group (A) andolanzapine group (B) by the Independent T-test showed that the positive symptom of the PANSSwas greater in group A than in group B significantly ($p < 0.05$), which was respectively 14.6% vs 8.5% on the 2nd week, 26.1% vs 19.1%.on the 4th week and 40.1 vs 31.0 on the 8th week. Result of the paired T-test for each group showed a significant decrease of the negative symptom of the PANSS ($p < 0.05$) since the 2nd week, in both groups. The longer the treatment, the greater the changes of the positive symptom of the PANSS which were 14.3% vs 11.5% on the 2nd week, 32.8% vs 24.3% on the 4th week and 48.1% vs 36.1% on the 8th week respectively.

Table 1. Comparison of Positive Symptom of the PANSS and Negative Symptom of the PANSS at Various Lengths of Treatment

Variable	Length of Treatment	Group		P*
		A	B	
		Mean(SD)% Changes	Mean(SD)% Changes	
Positive PANSS	the 2nd week	14.6(8.6)%	8.5(5.7)%	0.029
	the 4th week	26.1(8.4)%	19.1(9.1)%	0.036
	the 8th week	40.1(11.7)%	31.0(8.9)%	0.024
Negative PANSS	the 2ndweek	14.3(8.4)%	11.5(7.1)%	0.318
	the 4th week	32.8(9.3)%	24.3(5.6)%	0.008
	the 8th week	48.1(11.1)%	36.1(6.9)%	0.001

* Paired T-test. A: risperidone group, B: olanzapine group. **Source:** Primary Data, 2018.

Paired T test was used to see change of the positive symptom of the PANSS in the two groups because the data was distributed normally. There was a significant decreased of the positive symptom of the PANSS ($p < 0.05$) since the 2nd week in both groups. The longer the treatment, the greater the changes of the positive symptom of the PANSS, which were 14.6% vs 8,5% on the 2nd week, 26.1% vs 19.1% on the 4th week and 40.1% vs 31.0% on the 8th week respectively.

Table 2. The Effects of Both Treatment Groups on Positive Symptom of the PANSS Changes in Various Lengths of Treatment

Group	Length of Treatment	Decreases of positive PANSS			P*
		PANSS Value	Changes	% Changes	
A	the 2nd week	24.33(8.36)	3.73(3.6)	14.6(8.6)%	0.001
		20.60(6.87)			
	the 4th week	24.33(8.36)	6.67(3.96)	26.1(8.4)%	<0.001
		17.67(5.51)			
	the 8th week	24.33(8.36)	10.07(4.71)	40.1(11.7)%	<0.001
		14.27(4.96)			
B	the 2nd week	21.20(7.89)	2.13(1.51)	8.5(5.7)%	<0.001
		20.87(6.42)			
	the 4th week	21.20(7.89)	4.47(2.48)	19.1(9.1)%	<0.001
		18.53(6.19)			
	the 8th week	21.20(7.89)	7.27(2.99)	31.0(8.9)	<0.001

* Paired T-test. A: Risperidone group, B: Olanzapine group. **Source:** Primary Data, 2018.

Result of the paired T-test for each group showed a significant changes of the negative symptom of the PANSS ($p < 0.05$) since the 2nd week. In both groups the longer the study, the greater the change of the positive symptom of the PANSS which were 14.3% vs 11.5% on the 2nd week, 32.8% vs 24.3% on the 4th week and 48.1% vs 36.1% on the 8th week respectively.

Table 3. Effects of Both Treatment Groups on Negative Symptom of the PANSS Changes in Various Lengths of Treatment

Group	Observation	Decrease of Negative PANSS			P*
		Values	Changes	% Changes	
A	the 2nd week	20.27(6.27)	2.80(2.40)	14.3(8.4)%	<0.001
		17.47(5.95)			
	the 4th week	20.27(6.27)	6.53(2.80)	32.8(9.3)%	<0.001
		13.73(5.04)			
	the 8th week	20.27(6.27)	9.93(4.71)	48.1(11.1)%	<0.001
		10.33(3.58)			
B	the 2nd week	21.20(7.89)	2.40(1.40)	11.5(7.1)%	<0.001
		18.80(7.19)			
	the 4th week	21.20(7.89)	4.93(1.58)	24.3(5.6)%	<0.001
		16.27(6.64)			
	the 8th week	21.20(7.89)	7.60(3.02)	36.1(6.9)%	<0.001

* Paired T-test. A: Risperidone group, B: Olanzapine group. **Source:** Primary Data, 2018

The difference in total PANSS score between the two groups was consistent ($p<0.05$). Comparison of the changes in the total PANSS score in groups A and B by the Independent T-test showed a reduction of total PANSS in both groups ($p > 0.05$).

Table 4. Effects of Both Treatment Groups on Total PANSS at Various Lengths of Treatment

Group	Observation	Decrease in Negative PANSS			P*
		Value	Change	% Change	
A	the 2nd week	105.4(18.8)	12.8(6.3)	11.8(5.0)%	<0.001
		92.6(15.7)			
	the 4th week	105.4(18.8)	23.6(7.6)	21.5(4.9)%	<0.001
		82.3(14.0)			
	the 8th week	105.4(18.8)	32.1(9.0)	30.0(4.3)%	<0.001
		73.2(11.5)			
B	the 2nd week	74.2(21.3)	11.7(8.0)	62.5(17.9)%	<0.001
		62.3(17.9)			
	the 4th week	74.2(21.3)	20.5(9.4)	53.7(15.7)%	<0.001
		53.7(15.7)			
	the 8th week	74.2(21.3)	28.4(2.5)	45.8(14.4)%	<0.001
		45.8(14.4)			

Discussion

This study showed that risperidone and olanzapine were both effective for the positive symptoms and the negative symptoms, but risperidone was superior in dealing with both positive and negative symptoms. Olanzapine, a thienobenzodiazepine derivative is an atypical antipsychotic drug which shows affinity for D1-D5 receptors, serotonergic receptor (5HT2, 3, 6), muscarinic receptors (subtypes 1-5), adrenergic receptors (alpha 1-2), and histaminergicreceptor (H1). Structurally, this drug resembles clozapine but has little difference in terms of its affinity. This drug is weaker than clozapine as alpha 1 and alpha 2 adrenergic agonists, and is slightly different as D2, D4, or 5HT2A receptor antagonists.[4]

Paired T-test was used to see the changes in the positive PANSS for both groups, and each group showed a significant decrease in positive PANSS ($p < 0.05$)on the 2nd week of therapy in both groups. The longer the treatment, the greater the changes in the positive symptom of the PANSS score,which were 14.6% vs 8.5% on the 2nd week, 26.1% vs 19.1% on the 4th week and 40.1% vs 31.0% on the 8th week of study. Risperidone and olanzapine improved of the positive symptoms inboth groups (risperidone group and olanzapine group) starting from the 2nd week to the 8th week ($p = 0.001$).

When the Independent T-test was used to see the difference of the positive symptom of the PANSS score between the group given risperidone and the group given olanzapine, different results were obtained. The decrease of the positive PANSS was greater in group A (given risperidone) than in group B (given olanzapine) significantly ($p < 0.05$)which were 14.6% vs 8.5% on the 2nd week, 26.1% vs 19.1% on the 4th week and 40.1% vs 31.0%.

The changes in the positive symptom of the PANSS score was higher in therisperidone group since the 2nd week ($p = 0.029$) and there were more clinical changes in the positive symptoms in the risperidone group compared to the olanzapine group onthe 8th week. This finding was consistent with previous study,[5] where risperidone have a greater affinity for D2 than olanzapine.

The paired T-test results for each group along the study showed a significant decrease in the total PANSS scores ($p < 0.05$), seen from the 2nd week for both groups. This suggests that risperidone and olanzapine were equally effective for the negative symptoms. It was seen that the longer the therapy was given, the greater the changes in the negative symptom of the PANSS, which were 14.3% vs 11.5% on the 2nd week, 32.8% vs 24.3% on the 4th weeks and 48.1% vs 36.1% on the 8th weeks.

This finding was not in consistent with the publication results,[6]on which those who received olanzapine was better for the negative symptoms compared to risperidone since the first 3 months of treatment. This might becaused by different sampling method, different subtypes of schizophrenic, where in this study most of the subjects were paranoid schizophrenia with positive symptoms dominated over negative symptoms and simplex schizophrenia with negative symptoms dominated over the positive symptoms thus affecting the assessment results. Another thing that might affect this outcome was the sampling which combined inpatients and outpatients, in where hospitalized patients were more often in acute phase and predominated with positive symptoms compared to the outpatients. In addition, the outpatients had more family attention and support than those who were hospitalized, thus affecting the results of the assessment of the negative symptoms. Due to the limitations of the study, were the author's ability, time of study and costs. There were several weaknesses in this study,the PANSS score was not measured regularly every week due to clinical symptoms of schizophrenia, and this study did not examine the side effects of medication and drug effects that was used to minimize the side effects.

Conclusions and Recommendations

This study showed that risperid one and olanzapine were effective for both the positive and the negative symptoms, but risperidone was better for both positive and negative symptoms. Subject who received risperidone experienced more positive and negative symptoms improvement compared to olanzapine. The researchers suggested that further studies should be carried out with bigger samples size and longer observation times. It was necessary to differentiate the treatment status of patients taken as a subjects whether they were outpatients or inpatients.

Ethical Clearance: Taken from Wahidin Sudirohusodo Hospital and Hasanuddin University committee

Source of Funding: This research was privately funded

Conflict of Interest: The authore declare that there are no conflict of interests.

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